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Attorney Docket No. 9368-6IP

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Olmsted et al.
Application Serial No.: 09/991,258
Filed: November 16, 2001
For: *Alphavirus Vectors and Virosomes with Modified HIV Genes for Use in Vaccines*

U.S. Patent No.: 6,783,939 B2
Issued: August 31, 2004

Date: December 3, 2004

Commissioner for Patents
Attn: Certificate of Correction Branch
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR ENTRY OF CERTIFICATE OF CORRECTION UNDER 35 U.S.C §254 AND 37 C.F.R. §1.322

Sir:

The Assignee of record for the above-referenced patent hereby requests, pursuant to 35 U.S.C §254 and 37 C.F.R. §1.322, that a Certificate of Correction be issued. This request is made in order to correct the mistakes incurred through the fault of the U.S. Patent and Trademark Office. No fee is believed due. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

The mistakes appearing in the patent are set forth with corrections on the Certificate of Correction enclosed herewith, with an additional copy thereof and a return post card.

Respectfully submitted,

Mary L. Miller

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Certificate of Mailing under 37 CFR 1.8

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Monica L. Croom

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PTO/SB/44 (04-04)
Approved for use through 04/30/2007. OMB 0651-0033
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,783,939 B2
DATED : August 31, 2004
INVENTOR(S) : Olmsted et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Column 167, claim 1 should read -- **1**. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Column 167, claim 2 should read -- **2**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- **3**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- **7**. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- **8**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing

an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 9 should read -- **9**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 169, claim 13 should read -- **13**. An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- **18**. A method of making the alphavirus replicon particle of claim **17**, comprising
a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:
(i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
(ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
(iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;
and with at least one of said helper RNAs lacking an alphavirus packaging signal;
wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;
(b) producing the alphavirus replicon particles in the helper cell; and
(c) collecting the alphavirus replicon particles from the helper cell. --

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PATENT NO. 6,783,939
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Column 167, claim 2 should read -- **2**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- **3**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- **7**. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- **8**. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing

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an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

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Column 169, claim 13 should read -- **13**. An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

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(ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
(iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;
and with at least one of said helper RNAs lacking an alphavirus packaging signal;
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